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FINNEGAN, HENDERSON, FARABOW, GARRETT &
DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

| EXAMINER |
|---|
| EPPS, JANET L |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | 11 |

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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/713,017 | Applicant(s) CHOULIKA ET AL. | |
|---|---|---|---|
| | Examiner Janet L. Epps | Art Unit 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 25-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 25-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Supplemental Action*

1. The prior Office Action mailed 2-22-02 was incomplete since it did not consider the merits of originally filed claim 1. The following action includes a consideration of the merits of claim 1, and the remaining claims. Applicant's response time is therefore restarted as of the mail date of this Action.

### *Drawings*

2. The drawings submitted with this application have been objected to by the Draftsperson, see the attached PTO-948 for details. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

### *Claim Objections*

3. Claims 1 and 26 are objected to because of the following informalities: Claim 1 is grammatically incorrect since the claim does not begin with the appropriate indefinite article *"A"* or *"An."* Claim 26 recites the phrase "wherein said retroelements comprise cis-acting region," this phrase lacks the indefinite article "a" before the term "cis-acting." Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "preferably a single recognition site which can be recognized by a recombinase," this phrase is vague and indefinite since the term "preferably" renders the claim indefinite, because it is unclear whether the limitations following this term are part of the claimed invention. See MPEP § 2173.05(d).

Additionally, claim 1 recites "[s]equence of synthetic or natural retroelements, in particular of retroviral DNA," this limitation is considered indefinite, since in the present instance, the instant claim recites the broad recitation "sequence of synthetic or natural retroelements," and the claim also recites "in particular of retroviral DNA," which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd.

App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

Claims 32-35 recite the limitation "said recognition site" in referring back to claim 25. There is insufficient antecedent basis for this limitation in the claim. Claim 25 recites a "recognition sequence."

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In the present case applicants claim the deposited biological material by its accession number, I-1599. However, the specification is not enabling without complete evidence either that the vector according to pMcreloxPL deposited under No. I-1599 recited in the claim is known and **readily available to the public** or complete evidence of the deposit of the biological material. The specification refers to the vector at various places, but does not state that all restrictions on the deposits will be irrevocably removed on issuance of a patent and that the deposit will be replaced if viable samples cannot be dispensed by the depository is require. In the absence of evidence showing that these strains are publicly available (i.e., deposited in compliance with 37 CFR 1.801-1.809) or can be isolated without undue experimentation, claim 39 is not supported by an enabling disclosure.

A suitable deposit for patent purposes would overcome this ground of rejection. Deposits should be made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit. The Examiner notes that, if Applicant argues that the vector is well known and readily available to the public, the claim drawn in part to the vector will only remain enforceable while the vector remains readily available to the public.

***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 25-38 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,200,800. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because both the issued patent and the claims 25-26, 29-32, 37 and 40 of the instant application are drawn to a nucleic acid molecule and a retroviral vector comprising retroelements that comprise a recombinant provirus, a nucleotide sequence of interest, and a recognition sequence for the elimination of proviral sequences in the recombinant provirus. However, although the claims of the issued patent and those of the instant application read on overlapping subject matter, the claims of the instant application are broader in scope than those recited in the issued patent. The claims of the issued patent represent a distinct species of

the broader genus of nucleic acid molecules and retroviral vectors encompassed by the instant claims. The claims of the issued patent are further limited to a defined class of retroviral vector, namely wherein the vector is a defective Moloney murine leukemia virus, and wherein the recognition sequence in said virus is in a U3 region of its 3' LTR, or in a U5 region of its 5' LTR.

According to MPEP § 2131.02, "A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." The species in that case will anticipate or render obvious the claimed genus. Therefore, the distinct species of retroviral vector and nucleic acid molecules recited in the issued patent render obvious the claims drawn to a broad genus of retroviral vector and nucleic acid molecules as recited in the instant application.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

12. Claims 1, 25-26, 29-32, 34, 36-37 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al.

Applicants claim a nucleic acid molecule comprising retroelements that comprise a recombinant provirus, wherein the nucleic acid molecule contains a nucleotide sequence of interest that can be integrated with the retrovirus, and may further contain a recognition sequence for a recombinase. The sequence of interest is integrated into the cis acting region of the retroviral element (the long terminal repeat or LTR), wherein it is integrated between the 5' and 3' LTR regions, the vector may further encode a recombinase, which is the CRE protein of bacteriophage P1 and the recognition sequence encodes a loxP element, the sequence required for recombination events directed by the Cre recombinase.

Anderson discloses retroviral vector constructions (see figures 1a-1d and 2a-b) which contain LTR elements, which express sequences of interest that are integrated into a cis acting region of the virus, which encodes selectable markers, and further comprises promoters and other control elements. Such vectors were modified to contain loxP elements (fig. 2a-b) for the removal of an intervening nucleotide sequence. The use of the Cre/loxP and FLP/FRT recombinase systems is disclosed (col. 7, lines 20-28) and the gene encoding the recombinase (either Cre or FLP) is part of the retroviral construct (col. 8, lines 38-56). The desirability of removing or eliminating the recombinase by the recombination event, along with a sequence of interest, is further disclosed (col. 8, lines 47-52). Furthermore, Anderson also describes the use of replication defective retroviral vectors (col. 11, lines 41-67).

Anderson et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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14. Claims 1, 25-26, 29-38 ~~1, 25-38~~ and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable Anderson et al. (US Patent 5,629,159) in view of Sun et al.

Applicants claim a nucleic acid molecule comprising retroelements as described above, and further wherein the vector may also comprise a recombinase (Cre protein) inserted between the 5' and 3' LTR, and wherein the sequence of interest may encode a polypeptide, an antisense RNA or a ribozyme.

The discussion of Anderson et al. set forth in the above rejection is incorporated here. Anderson et al. does not specifically teach wherein the Cre recombinase is inserted between the 5' LTR and the 3' LTR, or wherein sequence of interest encodes for either an antisense RNA or a ribozyme. However, Anderson et al. disclose retroviral vectors comprising a STOP sequence, which prevents the translation of a selectable marker (col. 7, lines 53-58).

It would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Anderson by replacing the STOP sequence described above with an antisense or ribozyme sequence to the selectable marker, wherein upon expression of the antisense or ribozyme sequence (as a gene of interest) the translation of the selectable marker is inhibited by the expression of these sequences. Furthermore, one of ordinary skill in the art at the time of filing would have been motivated to make this modification since it appears that the

STOP sequence of Anderson et al. and an antisense or ribozyme sequence are functionally equivalent, since they both serve to inhibit the translation of a gene. It would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of have been obvious to replace one functionally equivalent sequence for another. Furthermore, Sun et al. provides sufficient guidance to direct the ordinary skilled artisan to design retroviral vector constructs comprising antisense or ribozymes inserted between two LTR retroelements (see Figure 1).

Additionally, it would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Anderson et al. to design the retroviral vectors according to the present invention wherein the retroviral vector comprises a nucleotide sequence coding for a recombinase that is situated between the 5' LTR and the 3' LTR. One of ordinary skill in the art would have been motivated to make the constructs according to the present invention because Anderson et al. discloses an alternative embodiment that incorporates this type of retroviral vector design. According to Anderson et al. Figure 6A describes a construct comprising an inducible promoter operably linked to a recombinase gene, wherein Figure 6A corresponds to Figure 1c with an inducible promoter/recombinase gene added, which will be left in the genome (col. 8, lines 38-55). When the construct according to 6A is incorporated into the design of the construct according to 1c, the inducible promoter and the recombinase gene is inserted after the second selection marker, wherein the insertion occurs between the 5' LTR and 3' LTR of the retroviral construct of Figure 1c. Additionally, Anderson et al. describes two recombinases that may be equally useful in these constructs, they include the Cre and FLP recombinases. The

sequence of either recombinase may be incorporated into the retroviral constructs of Anderson et al. (col. 7, lines 21-26).

Given the teachings of the prior art and the knowledge of one of ordinary skill in the art, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention. Therefore, the invention as a whole was *prima face* obvious at the time of filing over Anderson et al. in view of Sun et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 8:30AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps-Ford, Ph.D.
Examiner
Art Unit 1635

*JLE*
August 15, 2002

# Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

## The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

### INFORMATION ON HOW TO EFFECT DRAWING CHANGES

**1. Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

**2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

**Timing of Corrections**

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.